WEST Search History

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DATE: Wednesday, November 02, 2005

Hide?	Set Name	Query	Hit Count
	DB=PGPB; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L8	L3 and cinnamonensis	0
☐	L7	L4 and cinnamonensis	18
☐	L6	L4 and ethylmalonate	2
☐	L5	L4 and ethymalonate	0
☐	L4	monensin same (gene cluster or polyketide synthase)	124
	DB=USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L3	monensin same (gene cluster or polyketide synthase)	76
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L2	monensin same (gene cluster or polyketide synthase)	200
☐	L1	monensin and (gene cluster or polyketide synthase)	227

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Search Results - Record(s) 1 through 2 of 2 returned.

☐ 1. Document ID: US 20040219645 A1

L6: Entry 1 of 2 File: PGPB Nov 4, 2004

PGPUB-DOCUMENT-NUMBER: 20040219645
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040219645 A1

TITLE: Polyketides and their synthesis

PUBLICATION-DATE: November 4, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Leadley, Peter Francis	Cambridge		GB
Staunton, James	Cambridge		GB
Oliynyk, Mark Yan	Cambridge		GB

US-CL-CURRENT: 435/76

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 2. Document ID: US 20040023342 A1

L6: Entry 2 of 2 File: PGPB Feb 5, 2004

PGPUB-DOCUMENT-NUMBER: 20040023342
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040023342 A1

TITLE: Polyketides and their synthesis

PUBLICATION-DATE: February 5, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Petkovic, Hrvoje	Cambridge		GB
Kendrew, Steven Gary	Cambridge		GB
Leadlay, Peter Francis	Cambridge		GB

US-CL-CURRENT: 435/75

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

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Search Results - Record(s) 1 through 18 of 18 returned.

☐ 1. Document ID: US 20050090461 A1

L7: Entry 1 of 18 File: PGPB Apr 28, 2005

PGPUB-DOCUMENT-NUMBER: 20050090461
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050090461 A1

TITLE: Polyketides and their synthesis

PUBLICATION-DATE: April 28, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Leadlay, Peter Francis	Cambridge	CT	GB
Staunton, James	Cambridge		GB
Cortes, Jesus	Cambridge		GB
McArthur, Hamish Alastair Irvine	Mystic		US

US-CL-CURRENT: 514/29; 536/7.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 2. Document ID: US 20050089982 A1

L7: Entry 2 of 18 File: PGPB Apr 28, 2005

PGPUB-DOCUMENT-NUMBER: 20050089982
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050089982 A1

TITLE: Polyketides and their synthesis

PUBLICATION-DATE: April 28, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Leadlay, Peter Francis	Cambridge		GB
Staunton, James	Cambridge		GB
Cortes, Jesus	Cambridge		GB

US-CL-CURRENT: 435/193; 435/252.3, 435/471

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 3. Document ID: US 20050080247 A1

L7: Entry 3 of 18 File: PGPB Apr 14, 2005

PGPUB-DOCUMENT-NUMBER: 20050080247
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050080247 A1

TITLE: Leinamycin biosynthesis gene cluster and its components and their uses

PUBLICATION-DATE: April 14, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Shen, Ben	Verona,	WI	US
Cheng, Yi-qiang	Milwaukee	WI	US
Tang, Gong-li	Davis	CA	US

US-CL-CURRENT: 536/23.2; 435/189, 435/193, 435/252.3, 435/320.1, 435/69.1, 435/75

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 4. Document ID: US 20050048536 A1

L7: Entry 4 of 18 File: PGPB Mar 3, 2005

PGPUB-DOCUMENT-NUMBER: 20050048536
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050048536 A1

TITLE: Gilvocarcin gene cluster, recombinant production and use thereof

PUBLICATION-DATE: March 3, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Rohr, Jurgen	Georgetown	KY	US
Fischer, Carsten	Lexington	KY	US

US-CL-CURRENT: 435/6; 435/105, 435/190, 435/320.1, 435/325, 435/69.1, 536/1.11, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 5. Document ID: US 20050003409 A1

L7: Entry 5 of 18 File: PGPB Jan 6, 2005

PGPUB-DOCUMENT-NUMBER: 20050003409
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050003409 A1

TITLE: Cloning genes from streptomyces cyaneogriseus subsp. noncyanogenus for biosynthesis of antibiotics and methods of use

PUBLICATION-DATE: January 6, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Huang, Chengjin	Fort Dodge	IA	US
Chaleff, Deborah T.	Pennington	NJ	US
Ruppen, Mark E.	Garnerville	NY	US
Stephens, Jerome	Mentone	AL	US

US-CL-CURRENT: 435/6; 435/193, 435/252.3, 435/320.1, 435/69.1, 435/75, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 6. Document ID: US 20040219645 A1

L7: Entry 6 of 18 File: PGPB Nov 4, 2004

PGPUB-DOCUMENT-NUMBER: 20040219645
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040219645 A1

TITLE: Polyketides and their synthesis

PUBLICATION-DATE: November 4, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Leadley, Peter Francis	Cambridge		GB
Staunton, James	Cambridge		GB
Oliynyk, Mark Yan	Cambridge		GB

US-CL-CURRENT: 435/76

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 7. Document ID: US 20040203119 A1

L7: Entry 7 of 18 File: PGPB Oct 14, 2004

PGPUB-DOCUMENT-NUMBER: 20040203119
PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040203119 A1

TITLE: Cell-free synthesis of polyketides

PUBLICATION-DATE: October 14, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Khosla, Chaitan	Palo Alto	CA	US
Pieper, Rembert	Washington	DC	US
Luo, Guanglin	Madison	CT	US
Cane, David E.	Providence	RI	US

US-CL-CURRENT: 435/75; 435/193, 435/252.3, 435/320.1, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 8. Document ID: US 20040161828 A1

L7: Entry 8 of 18 File: PGPB Aug 19, 2004

PGPUB-DOCUMENT-NUMBER: 20040161828
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040161828 A1

TITLE: Gene cluster for production of the enediyne antitumor antibiotic C-1027

PUBLICATION-DATE: August 19, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Shen, Ben	Davis	CA	US
Liu, Wen	Tiantan	CA	CN
Christenson, Stephen D.	Davis		US
Standage, Scott	Bornet		GB

US-CL-CURRENT: 435/75; 435/105, 435/189, 435/191, 435/252.3, 435/320.1, 435/325, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 9. Document ID: US 20040023342 A1

L7: Entry 9 of 18 File: PGPB Feb 5, 2004

PGPUB-DOCUMENT-NUMBER: 20040023342
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040023342 A1

TITLE: Polyketides and their synthesis

PUBLICATION-DATE: February 5, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Petkovic, Hrvoje	Cambridge		GB
Kendrew, Steven Gary	Cambridge		GB
Leadlay, Peter Francis	Cambridge		GB

US-CL-CURRENT: 435/75

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Ds

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☐ 10. Document ID: US 20030225006 A1

L7: Entry 10 of 18 File: PGPB Dec 4, 2003

PGPUB-DOCUMENT-NUMBER: 20030225006
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030225006 A1

TITLE: Novel spinosyn-producing polyketide synthases

PUBLICATION-DATE: December 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Burns, Lesley S.	Cambridge	IN	GB
Graupner, Paul R.	Carmel	IN	US
Lewer, Paul	Indianapolis	IN	US
Martin, Christine J.	Cambridge		GB
Vousden, William A.	Dry Drayton		GB
Waldron, Clive	Indianapolis		US
Wilkinson, Barrie	Sharnbrook		GB

US-CL-CURRENT: 514/28; 536/7.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Ds

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☐ 11. Document ID: US 20030203425 A1

L7: Entry 11 of 18 File: PGPB Oct 30, 2003

PGPUB-DOCUMENT-NUMBER: 20030203425
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030203425 A1

TITLE: Hybrid glycosylated products and their production and use

PUBLICATION-DATE: October 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Leadlay, Peter Francis	Gaupe Rd Cambridge		GB
Staunton, James	Cambridge		GB
Gaisser, Sabine	Cambridge		GB

US-CL-CURRENT: 435/68.1; 435/101, 435/193, 435/75

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 12. Document ID: US 20030175888 A1

L7: Entry 12 of 18 File: PGPB Sep 18, 2003

PGPUB-DOCUMENT-NUMBER: 20030175888
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030175888 A1

TITLE: Discrete acyltransferases associated with type I polyketide synthases and methods of use

PUBLICATION-DATE: September 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Shen, Ben	Verona	WI	US
Cheng, Yi-Qiang	Madison	WI	US
Tang, Gong-Li	Madison	WI	US

US-CL-CURRENT: 435/69.1; 435/134, 435/252.3, 435/320.1, 435/471

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 13. Document ID: US 20030157654 A1

L7: Entry 13 of 18 File: PGPB Aug 21, 2003

PGPUB-DOCUMENT-NUMBER: 20030157654
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030157654 A1

TITLE: Biosynthesis of enediyne compounds by manipulation of C-1027 gene pathway

PUBLICATION-DATE: August 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Shen, Ben	Verona	WI	US
Liu, Wen	Madison	WI	US

US-CL-CURRENT: 435/78; 424/178.1, 514/28, 536/7.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 14. Document ID: US 20030068677 A1

L7: Entry 14 of 18 File: PGPB Apr 10, 2003

PGPUB-DOCUMENT-NUMBER: 20030068677
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030068677 A1

TITLE: Recombinant production of novel polyketides

PUBLICATION-DATE: April 10, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Khosla, Chaitan	Palo Alto	CA	US
Kao, Camilla M.	Palo Alto	CA	US

US-CL-CURRENT: 435/69.1; 435/193, 435/254.2, 435/320.1, 435/484

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 15. Document ID: US 20020110874 A1

L7: Entry 15 of 18 File: PGPB Aug 15, 2002

PGPUB-DOCUMENT-NUMBER: 20020110874
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020110874 A1

TITLE: Recombinant production of novel polyketides

PUBLICATION-DATE: August 15, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Khosla, Chaitan	Stanford	CA	US
Hopwood, David A.	Norwich	CA	GB
Ebert-Khosla, Susanne	Stanford	CA	US
McDaniel, Robert	Palo Alto	CA	US
Fu, Hong	Stanford	CA	US
Kao, Camilla	Stanford		US

US-CL-CURRENT: 435/76; 435/252.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 16. Document ID: US 20020004487 A1

L7: Entry 16 of 18 File: PGPB Jan 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020004487
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020004487 A1

TITLE: Novel erythromycins and process for their preparation

PUBLICATION-DATE: January 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Leadlay, Peter Francis	Cambridge		GB
Staunton, James	Cambridge		GB
Cortes, Jesus	Cambridge		GB
Pacey, Michael Stephen	Broadstairs		GB

US-CL-CURRENT: 514/29; 536/7.2, 536/7.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

☐ 17. Document ID: US 20010039021 A1

L7: Entry 17 of 18 File: PGPB Nov 8, 2001

PGPUB-DOCUMENT-NUMBER: 20010039021
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010039021 A1

TITLE: Recombinant production of novel

PUBLICATION-DATE: November 8, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Khosla, Chaitan	Stanford	CA	US
Hopwood, David A.	Norwich	CA	GB
Ebert-Khosla, Suzanne	Stanford	CA	US
McDaniel, Robert	Palo Alto	CA	US
Fu, Hong	Stanford	CA	US
Kao, Camilla	Stanford		US

US-CL-CURRENT: 435/7.1; 435/76

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

☐ 18. Document ID: US 20010016598 A1

L7: Entry 18 of 18 File: PGPB Aug 23, 2001

PGPUB-DOCUMENT-NUMBER: 20010016598
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010016598 A1

TITLE: ERYTHROMYCINS AND PROCESS FOR THEIR PREPARATION

PUBLICATION-DATE: August 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
LEADLAY, PETER FRANCIS	CAMBRIDGE		GB
STAUNTON, JAMES	CAMBRIDGE		GB
CORTES, JESUS	CAMBRIDGE		GB
PACEY, MICHAEL STEPHEN	BROADSTAIRS		GB

US-CL-CURRENT: 514/450

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 1. Document ID: US 6960453 B1

Using default format because multiple data bases are involved.

L3: Entry 1 of 76 File: USPT Nov 1, 2005

US-PAT-NO: 6960453
DOCUMENT-IDENTIFIER: US 6960453 B1

TITLE: Hybrid polyketide synthases combining heterologous loading and extender modules

DATE-ISSUED: November 1, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leadlay; Peter Francis	Cambridge			GB
Staunton; James	Cambridge			GB
Cortes; Jesus	Cambridge			GB

US-CL-CURRENT: 435/76; 435/183, 435/252.3, 435/252.35, 435/320.1, 435/471, 536/23.1, 536/23.2, 536/23.7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

☐ 2. Document ID: US 6949369 B2

L3: Entry 2 of 76 File: USPT Sep 27, 2005

US-PAT-NO: 6949369
DOCUMENT-IDENTIFIER: US 6949369 B2

TITLE: .alpha.-galactosidases and methods for making and using them

DATE-ISSUED: September 27, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Murphy; Dennis	Malvern	PA		
Reid; John	Ardmore	PA		
Robertson; Dan E.	San Diego	CA		

US-CL-CURRENT: 435/99; 435/18, 435/208, 435/252.3, 435/320.1, 435/69.1, 530/350,

536/23.2

ABSTRACT:

The invention relates to .alpha.-galactosidase and to polynucleotides encoding the .alpha.-galactosidase. In addition methods of designing new .alpha.-galactosidases and method of use thereof are also provided. The .alpha.-galactosidases have increased activity and stability at increased pH and temperature.

20 Claims, 7 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 3. Document ID: US 6943001 B2

L3: Entry 3 of 76 File: USPT Sep 13, 2005

US-PAT-NO: 6943001
DOCUMENT-IDENTIFIER: US 6943001 B2

TITLE: Epoxide hydrolases, nucleic acids encoding them and methods for making and using them

DATE-ISSUED: September 13, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Zhao; Lishan	Carlsbad	CA		
Mathur; Eric J.	Carlsbad	CA		
Weiner; David	Del Mar	CA		
Richardson; Toby	San Diego	CA		
Milan; Aileen	San Diego	CA		
Burk; Mark J.	San Diego	CA		
Han; Bin	San Diego	CA		
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/195; 435/18, 435/252.3, 435/254.1, 435/255.1, 435/320.1, 435/325, 435/410, 536/23.2, 536/24.33

ABSTRACT:

The invention is directed to polypeptides having epoxide hydrolase activity, polynucleotides encoding the polypeptides, antibodies that bind to these polypeptides, and methods for making and using these polynucleotides and polypeptides. The epoxide hydrolases are used to catalyze the hydrolysis of epoxides and arene oxides to their corresponding diols.

58 Claims, 19 Drawing figures
Exemplary Claim Number: 1

Number of Drawing Sheets: 14

☐ 4. Document ID: US 6939689 B2

L3: Entry 4 of 76 File: USPT Sep 6, 2005

US-PAT-NO: 6939689
DOCUMENT-IDENTIFIER: US 6939689 B2

TITLE: Exonuclease-mediated nucleic acid reassembly in directed evolution

DATE-ISSUED: September 6, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Djavakhishvili; Tsotne David	San Diego	CA		
Frey; Gerhard Johann	San Diego	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of exonuclease-mediated reassembly methods is the ability to reassemble nucleic acid strands that would otherwise be problematic to chimerize. Exonuclease-mediated reassembly methods can be used in combination with other mutagenesis methods provided herein. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

11 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

☐ 5. Document ID: US 6927286 B1

L3: Entry 5 of 76 File: USPT Aug 9, 2005

US-PAT-NO: 6927286
DOCUMENT-IDENTIFIER: US 6927286 B1

TITLE: Bleomycin gene cluster components and their uses

DATE-ISSUED: August 9, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Shen; Ben	Davis	CA		
Du; Liangcheng	Davis	CA		
Sanchez; Cesar	Asturias			ES
Chen; Mei	Davis	CA		
Edwards; Daniel J.	Davis	CA		

US-CL-CURRENT: 536/23.2; 435/252.3, 435/252.35, 435/254.11, 435/320.1, 435/325, 435/419, 536/23.1, 536/23.7

ABSTRACT:

This invention provides detailed sequence analysis and characterization of the gene cluster responsible for the synthesis of bleomycin in Streptomyces verticillus. The bleomycin gene cluster provides the first hybrid polyketide synthase/nonribosomal peptide synthetase pathway and elucidation of the various modules and enzymatic domains characterizing the pathway provides convenient synthetic routes for bleomycins, bleomycin analogs, and various other polyketides.

10 Claims, 28 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 19

☐ 6. Document ID: US 6927057 B2

L3: Entry 6 of 76 File: USPT Aug 9, 2005

US-PAT-NO: 6927057
DOCUMENT-IDENTIFIER: US 6927057 B2

TITLE: Macrolide analogs

DATE-ISSUED: August 9, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Palo Alto	CA		

Ashley; Gary	Alameda	CA
Kao; Camilla M.	Palo Alto	CA
McDaniel; Robert	Palo Alto	CA

US-CL-CURRENT: 435/253.5; 435/183, 435/41, 435/76, 514/29, 536/7.1

ABSTRACT:

Combinatorial libraries of polyketides can be obtained by suitable manipulation of a host modular polyketide synthase gene cluster such as that which encodes the PKS for erythromycin. The combinatorial library is useful as a source of pharmaceutically active compounds. In addition, novel polyketides and antibiotics are prepared using this method.

8 Claims, 24 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 22

☐ 7. Document ID: US 6872526 B2

L3: Entry 7 of 76 File: USPT Mar 29, 2005

US-PAT-NO: 6872526
DOCUMENT-IDENTIFIER: US 6872526 B2

TITLE: High throughput screening for novel Bioactivities

DATE-ISSUED: March 29, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Keller; Martin	San Diego	CA		

US-CL-CURRENT: 435/6; 435/252.33, 435/252.35, 435/471, 435/476, 435/484, 435/486

ABSTRACT:

Disclosed is a process for identifying clones having a specified activity of interest, which process comprises (i) generating one or more expression libraries derived from nucleic acid directly isolated from the environment; and (ii) screening said libraries utilizing a fluorescence activated cell sorter to identify said clones. More particularly, this is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; (ii) exposing said libraries to a particular substrate or substrates of interest; and (iii) screening said exposed libraries utilizing a fluorescence activated cell sorter to identify clones which react with the substrate or substrates. Also provided is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; and (ii) screening said

exposed libraries utilizing an assay requiring co-encapsulation, a binding event or the covalent modification of a target, and a fluorescence activated cell sorter to identify positive clones.

42 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 8. Document ID: US 6866824 B2

L3: Entry 8 of 76 File: USPT Mar 15, 2005

US-PAT-NO: 6866824
DOCUMENT-IDENTIFIER: US 6866824 B2

TITLE: Capillary array-based sample screening

DATE-ISSUED: March 15, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lafferty; William Michael	Encinitas	CA		
Short; Jay M.	Rancho Santa Fe	CA		
Keller; Martin	San Diego	CA		

US-CL-CURRENT: 422/82.05; 422/82.09, 422/82.11, 436/165

ABSTRACT:

Provided are methods of screening and identification of bioactivities and bioactive molecules of interest using a capillary array system. More specifically, disclosed are methods of using optical detection and capillary array-based techniques for screening libraries and recovering bioactive molecules having a desired activity or a nucleic acid sequence encoding such bioactive molecules.

2 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 17

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 9. Document ID: US 6855525 B1

L3: Entry 9 of 76 File: USPT Feb 15, 2005

US-PAT-NO: 6855525
DOCUMENT-IDENTIFIER: US 6855525 B1

TITLE: Method for producing optically active 4-halo-3-hydroxybutyric acid ester

DATE-ISSUED: February 15, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Yamamoto; Hiroaki	Ibaraki			JP

US-CL-CURRENT: 435/135; 435/183, 435/189, 435/280

ABSTRACT:

The present invention provides a method for preparing (S)-4-halo-3-hydroxybutyric acid ester comprises asymmetric reduction of 4-halo-acetoacetic acid ester using .beta.-ketoacyl-acylcarrier protein reductase constituting Type II fatty acid synthase or acetoacetyl-CoA reductase constituting the poly-.beta.-hydroxy fatty acid synthesis system. .beta.-ketoacyl-acyl carrier protein reductase constituting Type II fatty acid synthase or acetoacetyl-CoA reductase constituting the poly-.beta.-hydroxy fatty acid synthesis system has a extremely high reducing activity as well as stereoseletivity for (S)-4-chloro-3-hydroxybutyric acid ester. In addition, the enzyme exhibits almost no oxidizing activity toward either configuration of ethyl 4-chloro-3-hydroxybutyrate, performing only the reducing reaction of ethyl, 4-chloroacetoacetate. Therefore, this enzyme can be used to efficiently produce (S)-4-halo-3-hydroxybutyric acid ester.

22 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

☐ 10. Document ID: US 6855365 B2

L3: Entry 10 of 76 File: USPT Feb 15, 2005

US-PAT-NO: 6855365
DOCUMENT-IDENTIFIER: US 6855365 B2

TITLE: Recombinant bacterial phytases and uses thereof

DATE-ISSUED: February 15, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Kretz; Keith A.	San Marcos	CA		
Gray; Kevin A.	San Diego	CA		
Barton; Nelson Robert	San Diego	CA		
Garrett; James B.	Poway	CA		
O'Donoghue; Eileen	San Diego	CA		
Mathur; Eric J.	Carlsbad	CA		

US-CL-CURRENT: 426/656; 435/18, 435/195, 435/196, 435/252.3, 435/320.1, 530/350, 536/23.2

ABSTRACT:

A purified and modified phytase enzyme from Escherichia coli K12 appA phytase is provided. The enzyme has phytase activity and improved thermal tolerance as compared with the wild-type enzyme. In addition, the enzyme has improved protease stability at low pH. Glycosylation of the modified phytase provided a further improved enzyme having improved thermal tolerance and protease stability. The enzyme can be produced from native or recombinant host cells and can be used to aid in the digestion of phytate where desired. In particular, the phytase of the present invention can be used in foodstuffs to improve the feeding value of phytate rich ingredients.

21 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 10

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 11. Document ID: US 6849395 B2

L3: Entry 11 of 76 File: USPT Feb 1, 2005

US-PAT-NO: 6849395
DOCUMENT-IDENTIFIER: US 6849395 B2

TITLE: Gene cluster screening of clones having DNA from mixed populations of organisms

DATE-ISSUED: February 1, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/4; 435/183, 435/6

ABSTRACT:

Disclosed is a process of screening clones having DNA from an uncultivated microorganism for a specified protein, e.g. enzyme, activity by screening for a specified protein, e.g. enzyme, activity in a library of clones prepared by (i) recovering DNA from a DNA population derived from at least one uncultivated microorganism; and (ii) transforming a host with recovered DNA to produce a library of clones which is screened for the specified protein, e.g. enzyme, activity.

8 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

☐ 12. Document ID: US 6846627 B2

L3: Entry 12 of 76 File: USPT Jan 25, 2005

US-PAT-NO: 6846627
DOCUMENT-IDENTIFIER: US 6846627 B2

TITLE: Screening for novel compounds which regulate biological interactions

DATE-ISSUED: January 25, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/6; 435/29

ABSTRACT:

Disclosed is a process for identifying compounds having a specified activity of interest, which process comprises (i) introducing interacting molecules into a host cell under conditions to generate or repress a detectable signal; and (ii) introducing a third compound or gene or genes encoding a third compound into the host cell from (i); and (iii) screening said host cell utilizing a method for detecting the inhibition or enhancement of interaction of proteins or other molecules in an in vivo or in vitro system. Another aspect of the present invention provides a process for identifying compounds of interest, which process comprises (i) generating one or more expression libraries derived from nucleic acid directly isolated from the environment; and (ii) screening said libraries utilizing a method for detecting the inhibition or enhancement of interaction of proteins or other molecules in an in vivo or in vitro system.

15 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

☐ 13. Document ID: US 6806048 B2

L3: Entry 13 of 76 File: USPT Oct 19, 2004

US-PAT-NO: 6806048
DOCUMENT-IDENTIFIER: US 6806048 B2

TITLE: Method for high throughput screening of an environmental library

DATE-ISSUED: October 19, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Keller; Martin	San Diego	CA		

US-CL-CURRENT: 435/6; 435/29, 435/69.1, 435/7.2

ABSTRACT:

Disclosed is a process for identifying clones having a specified activity of interest, which process comprises (i) generating one or more expression libraries derived from nucleic acid directly isolated from the environment; and (ii) screening said libraries utilizing a fluorescence activated cell sorter to identify said clones. More particularly, this is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; (ii) exposing said libraries to a particular substrate or substrates of interest; and (iii) screening said exposed libraries utilizing a fluorescence activated cell sorter to identify clones which react with the substrate or substrates. Also provided is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; and (ii) screening said exposed libraries utilizing an assay requiring co-encapsulation, a binding event or the covalent modification of a target, and a fluorescence activated cell sorter to identify positive clones.

15 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

☐ 14. Document ID: US 6794127 B1

L3: Entry 14 of 76 File: USPT Sep 21, 2004

US-PAT-NO: 6794127
DOCUMENT-IDENTIFIER: US 6794127 B1

TITLE: Capillary array-based sample screening

DATE-ISSUED: September 21, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lafferty; William Michael	Encinitas	CA		
Short; Jay M.	Rancho Santa Fe	CA		
Keller; Martin	San Diego	CA		

US-CL-CURRENT: 435/4; 435/183, 435/6

ABSTRACT:

Provided are methods of screening and identification of bio activities and bioactive molecules of interest using a capillary array system. More specifically, disclosed are methods of using optical detection and capillary array-based techniques for screening libraries and recovering bioactive molecules having a desired activity or a nucleic acid sequence encoding such bioactive molecules.

56 Claims, 20 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 17

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 15. Document ID: US 6790605 B1

L3: Entry 15 of 76 File: USPT Sep 14, 2004

US-PAT-NO: 6790605
DOCUMENT-IDENTIFIER: US 6790605 B1

TITLE: Methods for obtaining a desired bioactivity or biomolecule using DNA libraries from an environmental source

DATE-ISSUED: September 14, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/4; 435/14, 435/15, 435/16, 435/18, 435/19, 435/21, 435/22, 435/23, 435/24, 435/6

ABSTRACT:

Disclosed is a process for obtaining an enzyme having a specified enzyme activity derived from a heterogeneous DNA population by screening, for the specified enzyme activity, a library of clones containing DNA from the heterogeneous DNA population which have been exposed to directed mutagenesis towards production of the specified enzyme activity. Also disclosed is a process for obtaining an enzyme having a specified enzyme activity by screening, for the specified enzyme activity, a library of clones containing DNA from a pool of DNA populations which have been exposed to directed mutagenesis in an attempt to produce in the library of clones DNA encoding an enzyme having one or more desired characteristics which can be the same or different from the specified enzyme activity.

21 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 16. Document ID: US 6773900 B2

L3: Entry 16 of 76 File: USPT Aug 10, 2004

US-PAT-NO: 6773900
DOCUMENT-IDENTIFIER: US 6773900 B2

TITLE: End selection in directed evolution

DATE-ISSUED: August 10, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Frey; Gerhard Johann	San Diego	CA		

US-CL-CURRENT: 435/69.1; 435/69.7, 435/7.6, 530/350

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of end-selection-based methods is the ability to recover full-length polynucleotides from a library of progeny molecules generated by mutagenesis methods. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

11 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 17. Document ID: US 6764835 B2

L3: Entry 17 of 76 File: USPT Jul 20, 2004

US-PAT-NO: 6764835
DOCUMENT-IDENTIFIER: US 6764835 B2

TITLE: Saturation mutageneis in directed evolution

DATE-ISSUED: July 20, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/69.1; 435/69.7, 435/7.6, 530/350

ABSTRACT:

Disclosed is a rapid and facilitated method of producing from a parentlal template polynucleotide, a set of mutagenized progeny polynculeotides whereby at each original codon position there is produced at least one substitute codon encoding each of the 20 naturally encoded amino acids. Accordingly, there is also provided a method of producing from a parental template polypeptide, a set of mutagenized progeny polypeptides wherein each of the 20 naturally encoded amino acids is represented at each original amino acid position. The method provided is termed site-saturation mutagenesis, or simply saturation mutagenesis, and can be used in combination with other mutagenization processes, such as, for example, a process wherein two or more related polynucleotides are introduced into a suitable host cell such that a hybrid polynucleotide is generated by recombination and reductive reassortment. Also provided are vector and expression vehicles incuding such polynucleotides, polypeptides expressed by the hybrid polynucleotides and a method for screening for hybrid polypeptides.

26 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 2

☐ 18. Document ID: US 6750040 B1

L3: Entry 18 of 76 File: USPT Jun 15, 2004

US-PAT-NO: 6750040
DOCUMENT-IDENTIFIER: US 6750040 B1

TITLE: Cell-free synthesis of polyketides

DATE-ISSUED: June 15, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Pieper; Rembert	Washington	DC		
Luo; Guanglin	Providence	RI		
Cane; David E.	Providence	RI		

US-CL-CURRENT: 435/41; 435/64

ABSTRACT:

Cell-free systems which effect the production of polyketides employing modular

polyketide synthases are described. Libraries of new and/or known polyketides may also be produced in cell-free systems employing aromatic PKS, modular PKS or both.

15 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 19. Document ID: US 6740506 B2

L3: Entry 19 of 76 File: USPT May 25, 2004

US-PAT-NO: 6740506
DOCUMENT-IDENTIFIER: US 6740506 B2

TITLE: End selection in directed evolution

DATE-ISSUED: May 25, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Frey; Gerhard Johann	San Diego	CA		

US-CL-CURRENT: 435/69.1; 435/69.7, 435/7.6, 530/350

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of end-selection-based methods is the ability to recover full-length polynucleotides from a library of progeny molecules generated by mutagenesis methods. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors, can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

4 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 20. Document ID: US 6720014 B1

L3: Entry 20 of 76 File: USPT Apr 13, 2004

US-PAT-NO: 6720014
DOCUMENT-IDENTIFIER: US 6720014 B1

TITLE: Phytase-containing foodstuffs and methods of making and using them

DATE-ISSUED: April 13, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Kretz; Keith A.	San Marcos	CA		

US-CL-CURRENT: 426/52; 426/53, 426/61, 426/615, 426/635, 435/18, 435/196, 435/320.1, 435/410, 435/468, 435/69.1, 536/23.2, 800/278, 800/295

ABSTRACT:

A purified recombinant phytase enzyme derived from Escherichia coli B. The enzyme has a molecular light of about 47.1 kilodaltons and has phytase activity. The enzyme can be produced from native or recombinant host cells and can be used to aid in the digestion of phytate where desired. In particular, the phytase of the present invention can be used in foodstuffs to improve the feeding value of phytate rich ingredients.

40 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. De

☐ 21. Document ID: US 6713282 B2

L3: Entry 21 of 76 File: USPT Mar 30, 2004

US-PAT-NO: 6713282
DOCUMENT-IDENTIFIER: US 6713282 B2

TITLE: End selection in directed evolution

DATE-ISSUED: March 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		
Frey; Gerhard Johann	San Diego	CA		

US-CL-CURRENT: 435/69.1; 435/6

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of end-selection-based methods is the ability to recover full-length polynucleotides from a library of progeny molecules generated by mutagenesis methods. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

29 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 22. Document ID: US 6713279 B1

L3: Entry 22 of 76 File: USPT Mar 30, 2004

US-PAT-NO: 6713279
DOCUMENT-IDENTIFIER: US 6713279 B1

TITLE: Non-stochastic generation of genetic vaccines and enzymes

DATE-ISSUED: March 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/69.1; 435/320.1, 435/334, 435/6

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by use of non-stochastic methods of directed evolution (DirectEvolution.TM.). These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). Through use of the claimed methods, genetic vaccines, enzymes, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit

increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

105 Claims, 73 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 64

☐ 23. Document ID: US 6709841 B2

L3: Entry 23 of 76 File: USPT Mar 23, 2004

US-PAT-NO: 6709841
DOCUMENT-IDENTIFIER: US 6709841 B2

TITLE: Exonuclease-mediated gene assembly in directed evolution

DATE-ISSUED: March 23, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

A directed evolution process comprising novel methods for generating improved progeny molecules having desirable properties, including, for example, a method for rapid and facilitated production from a parental polynucleotide template, of a set of mutagenized progeny polynucleotides wherein at least one codon encoding each of the 20 naturally encoded amino acids is represented at each original codon position. This method, termed site-saturation mutagenesis, or simply saturation mutagenesis, is preferably based on the use of the degenerate N,N,G/T sequence. Also, a method of producing from a parental polypeptide template, a set of mutagenized progeny polypeptides wherein each of the 20 naturally encoded amino acids is represented at each original amino acid position. Also, other mutagenization processes that can be used in combination with, or in lieu of, saturation mutagenesis, including, for example: (a) assembly and/or reassembly of polynucloetide building blocks (including sections of genes &/or of gene families) mediated by a source of exonuclease activity such as exonuclease III; and (b) introduction of two or more related polynucleotides into a suitable host cell such that a hybrid polynucleotide is generated by recombination and reductive reassortment. Also molecular property screening methods, including a preferred method, termed end selection, comprised of using an enzyme, such as a topoisomerase, a restriction endonuclease, &/or a nicking enzyme (such as N. BstNB I), to detect a specific terminal sequence in a working polynucleotide, to produce a ligatable end thereat, and to ligate and clone the working polynucleotide.

18 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw

☐ 24. Document ID: US 6696275 B2

L3: Entry 24 of 76 File: USPT Feb 24, 2004

US-PAT-NO: 6696275
DOCUMENT-IDENTIFIER: US 6696275 B2

TITLE: End selection in directed evolution

DATE-ISSUED: February 24, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Frey; Gerhard Johann	San Diego	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

A directed evolution process comprising novel methods for generating improved progeny molecules having desirable properties, including, for example, a method for rapid and facilitated production from a parental polynucleotide template, of a set of mutagenized progeny polynucleotides wherein at least one codon encoding each of the 20 naturally encoded amino acids is represented at each original codon position. This method, termed site-saturation mutagenesis, or simply saturation mutagenesis, is preferably based on the use of the degenerate N,N,G/T sequence. Also, a method of producing from a parental polypeptide template, a set of mutagenized progeny polypeptides wherein each of the 20 naturally encoded amino acids is represented at each original amino acid position. Also, other mutagenization processes that can be used in combination with, or in lieu of, saturation mutagenesis, including, for example: (a) assembly and/or reassembly of polynucloetide building blocks, which building blocks can be sections of genes &/or of gene families; and (b) introduction of two or more related polynucleotides into a suitable host cell such that a hybrid polynucleotide is generated by recombination and reductive reassortment. Also, vector and expression vehicles including such polynucleotides and correspondingly expressed polypeptides. Also molecular property screening methods, including a preferred method, termed end selection, comprised of using an enzyme, such as a topoisomerase, a restriction endonuclease, &/or a nicking enzyme (such as N. BstNB I), to detect a specific terminal sequence in a working polynucleotide, to produce a ligatable end thereat, and to ligate and clone the working polynucleotide.

15 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

☐ 25. Document ID: US 6677115 B2

L3: Entry 25 of 76 File: USPT Jan 13, 2004

US-PAT-NO: 6677115
DOCUMENT-IDENTIFIER: US 6677115 B2

TITLE: Protein activity screening of clones having DNA from uncultivated microorganisms

DATE-ISSUED: January 13, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/4; 435/6

ABSTRACT:

Disclosed is a process of screening clones having DNA from an uncultivated microorganism for a specified protein, e.g. enzyme, activity by screening for a specified protein, e.g. enzyme, activity in a library of clones prepared by (i) recovering DNA from a DNA population derived from at least one uncultivated microorganism; and (ii) transforming a host with recovered DNA to produce a library of clones which is screened for the specified protein, e.g. enzyme, activity.

27 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

☐ 26. Document ID: US 6635449 B2

L3: Entry 26 of 76 File: USPT Oct 21, 2003

US-PAT-NO: 6635449
DOCUMENT-IDENTIFIER: US 6635449 B2

TITLE: Exonuclease-mediated nucleic acid reassembly in directed evolution

DATE-ISSUED: October 21, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of exonuclease-mediated reassembly methods is the ability to reassemble nucleic acid strands that would otherwise be problematic to chimerize. Exonuclease-mediated reassembly methods can be used in combination with other mutagenesis methods provided herein. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

17 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

☐ 27. Document ID: US 6632600 B1

L3: Entry 27 of 76 File: USPT Oct 14, 2003

US-PAT-NO: 6632600
DOCUMENT-IDENTIFIER: US 6632600 B1

TITLE: Altered thermostability of enzymes

DATE-ISSUED: October 14, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/4; 435/14, 435/15, 435/16, 435/18, 435/19, 435/21, 435/22, 435/23, 435/24, 435/25, 435/26, 435/27, 435/28, 435/6

ABSTRACT:

Provided is a method of screening gene libraries derived from a mixed population of organisms for a bioactivity or biomolecule of interest. The mixed population of organisms can be a cultured population or an uncultured population from, for example, the environment. Also provided are methods of screening isolates or enriched populations of organisms, which isolates include a population that is spatially, temporally, or hierarchical, for example, of a particular species, genus, family, or class of organisms. Identified clones containing a biomolecule or

bioactivity of interest can be further variegated or the DNA contained in the clone can be variegated to create novel biomolecules or bioactivities of interest.

61 Claims, 0 Drawing figures
Exemplary Claim Number: 1

☐ 28. Document ID: US 6605449 B1

L3: Entry 28 of 76 File: USPT Aug 12, 2003

US-PAT-NO: 6605449
DOCUMENT-IDENTIFIER: US 6605449 B1

TITLE: Synthetic ligation reassembly in directed evolution

DATE-ISSUED: August 12, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/69.1; 435/6

ABSTRACT:

Harvesting the full richness of biodiversity is instantly recognized by Diversa Corporation as a powerful means to access both novel molecules having direct commercial utility as well as molecular templates that could be retooled to acquire commercial utility. A directed evolution process for rapid and facilitated production from a progenitor polynucleotide template, of a library of mutagenized progeny polynucleotides wherein each of the 20 naturally encoded amino acids is encoded at each original codon position. This method, termed site-saturation mutagenesis, or simply saturation mutagenesis, is preferably based on the use of the degenerate N,N,G/T sequence. Also, a method of non-stochastically producing a library of chimeric nucleic acid molecules having an overall assembly order that is chosen by design. Accordingly, a set of progenitor templates, such as genes (e.g. a family of esterase genes) or genes pathways (e.g. encoding antibiotics) can be shuffled to generate a sizable library of distinct progeny polynucleotide molecules (e.g. 10.sup.100) and correspondingly encoded polypeptides. Screening of these polynucleotide libraries enables the identification of a desirable molecular species that has a desirable property, such as a specific enzymatic activity serviceable for a commercial application, or a novel antibiotic. Also, a method of retooling genes and gene pathways by the introduction of regulatory sequences, such as promoters, that are operable in an intended host, thus conferring operability to a novel gene pathway when it is introduced into an intended host. For example a novel man-made gene pathway, generated based on microbially-derived progenitor templates, that is operable in a plant cell.

12 Claims, 32 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 30

☐ 29. Document ID: US 6602675 B2

L3: Entry 29 of 76 File: USPT Aug 5, 2003

US-PAT-NO: 6602675
DOCUMENT-IDENTIFIER: US 6602675 B2

TITLE: High throughput screening of mycelia for bioactivities or biomolecules

DATE-ISSUED: August 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Keller; Martin	San Diego	CA		

US-CL-CURRENT: 435/7.32; 435/4, 435/7.4

ABSTRACT:

Disclosed is a process for identifying clones having a specified activity of interest, which process comprises (i) generating one or more expression libraries derived from nucleic acid directly isolated from the environment; and (ii) screening said libraries utilizing a fluorescence activated cell sorter to identify said clones. More particularly, this is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; (ii) exposing said libraries to a particular substrate or substrates of interest; and (iii) screening said exposed libraries utilizing a fluorescence activated cell sorter to identify clones which react with the substrate or substrates. Also provided is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; and (ii) screening said exposed libraries utilizing an assay requiring co-encapsulation, a binding event or the covalent modification of a target, and a fluorescence activated cell sorter to identify positive clones.

10 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

☐ 30. Document ID: US 6562594 B1

L3: Entry 30 of 76 File: USPT May 13, 2003

US-PAT-NO: 6562594
DOCUMENT-IDENTIFIER: US 6562594 B1

TITLE: Saturation mutagenesis in directed evolution

DATE-ISSUED: May 13, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/69.1; 435/69.7, 435/7.6, 530/350

ABSTRACT:

Disclosed is a rapid and facilitated method of producing from a parentlal template polynucleotide, a set of mutagenized progeny polynculeotides whereby at each original codon position there is produced at least one substitute codon encoding each of the 20 naturally encoded amino acids. Accordingly, there is also provided a method of producing from a parental template polypeptide, a set of mutagenized progeny polypeptides wherein each of the 20 naturally encoded amino acids is represented at each original amino acid position. The method provided is termed site-saturation mutagenesis, or simply saturation mutagenesis, and can be used in combination with other mutagenization processes, such as, for example, a process wherein two or more related polynucleotides are introduced into a suitable host cell such that a hybrid polynucleotide is generated by recombination and reductive reassortment. Also provided are vector and expression vehicles incuding such polynucleotides, polypeptides expressed by the hybrid polynucleotides and a method for screening for hybrid polypeptides.

6 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 2

Terms	Documents
monensin same (gene cluster or polyketide synthase)	76

Hit List

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Search Results - Record(s) 31 through 60 of 76 returned.

☐ 31. Document ID: US 6558942 B1

Using default format because multiple data bases are involved.

L3: Entry 31 of 76 File: USPT May 6, 2003

US-PAT-NO: 6558942
DOCUMENT-IDENTIFIER: US 6558942 B1
** See image for Certificate of Correction **

TITLE: Combinatorial polyketide libraries produced using a modular PKS gene cluster as scaffold

DATE-ISSUED: May 6, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Palo Alto	CA		
Kao; Camilla M.	Palo Alto	CA		

US-CL-CURRENT: 435/253.5; 435/4, 435/41, 435/76, 514/29, 536/7.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | [illegible] | Claims | KWIC | Draw De

☐ 32. Document ID: US 6555315 B1

L3: Entry 32 of 76 File: USPT Apr 29, 2003

US-PAT-NO: 6555315
DOCUMENT-IDENTIFIER: US 6555315 B1

TITLE: Screening for novel bioactivities

DATE-ISSUED: April 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/6; 435/440, 435/455, 435/91.1, 435/91.2, 436/501, 536/23.1, 536/24.3, 536/24.31, 536/24.32, 536/24.33

ABSTRACT:

Disclosed is a process for identifying clones having a specified activity of interest, which process comprises (i) generating one or more expression libraries derived from nucleic acid directly isolated from the environment; and (ii) screening said libraries utilizing an assay system. More particularly, this is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; (ii) exposing said libraries to a particular substrate or substrates of interest; and (iii) screening said exposed libraries utilizing a fluorescence activated cell sorter to identify clones which react with the substrate or substrates. Also provided is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; and (ii) screening said exposed libraries utilizing an assay requiring a binding event or the covalent modification of a target, and a fluorescence activated cell sorter to identify positive clones.

14 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

☐ 33. Document ID: US 6537776 B1

L3: Entry 33 of 76 File: USPT Mar 25, 2003

US-PAT-NO: 6537776
DOCUMENT-IDENTIFIER: US 6537776 B1

TITLE: Synthetic ligation reassembly in directed evolution

DATE-ISSUED: March 25, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

Harvesting the full richness of biodiversity is instantly recognized by Diversa Corporation as a powerful means to access both novel molecules having direct commercial utility as well as molecular templates that could be retooled to acquire commercial utility. A directed evolution process for rapid and facilitated production from a progenitor polynucleotide template, of a library of mutagenized progeny polynucleotides wherein each of the 20 naturally encoded amino acids is encoded at each original codon position. This method, termed site-saturation mutagenesis, or simply saturation mutagenesis, is preferably based on the use of the degenerate N,N,G/T sequence. Also, a method of non-stochastically producing a library of chimeric nucleic acid molecules having an overall assembly order that is chosen by design. Accordingly, a set of progenitor templates, such as genes (e.g. a family of esterase genes) or genes pathways (e.g. encoding antibiotics) can be shuffled to generate a sizable library of distinct progeny polynucleotide molecules

(e.g. 10.sup.100) and correspondingly encoded polypeptides. Screening of these polynucleotide libraries enables the identification of a desirable molecular species that has a desirable property, such as a specific enzymatic activity serviceable for a commercial application, or a novel antibiotic. Also, a method of retooling genes and gene pathways by the introduction of regulatory sequences, such as promoters, that are operable in an intended host, thus conferring operability to a novel gene pathway when it is introduced into an intended host. For example a novel man-made gene pathway, generated based on microbially-derived progenitor templates, that is operable in a plant cell.

15 Claims, 20 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 18

☐ 34. Document ID: US 6531299 B1

L3: Entry 34 of 76 File: USPT Mar 11, 2003

US-PAT-NO: 6531299
DOCUMENT-IDENTIFIER: US 6531299 B1

TITLE: Cell-free synthesis of polyketides

DATE-ISSUED: March 11, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Pieper; Rembert	Washington	DC		
Luo; Guanglin	Providence	RI		
Cane; David E.	Providence	RI		

US-CL-CURRENT: 435/75; 435/76, 435/77, 435/78, 435/79, 435/80, 435/81, 435/82, 435/83

ABSTRACT:

Cell-free systems which effect the production of polyketides employing modular polyketide synthases are described. Libraries of new and/or known polyketides may also be produced in cell-free systems employing aromatic PKS, modular PKS or both.

15 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 35. Document ID: US 6528249 B1

L3: Entry 35 of 76 File: USPT Mar 4, 2003

US-PAT-NO: 6528249
DOCUMENT-IDENTIFIER: US 6528249 B1

TITLE: Protein activity screening of clones having DNA from uncultivated microorganisms

DATE-ISSUED: March 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/4; 435/6

ABSTRACT:

Disclosed is a process of screening clones having DNA from an uncultivated microorganism for a specified protein, e.g. enzyme, activity by screening for a specified protein, e.g. enzyme, activity in a library of clones prepared by (i) recovering DNA from a DNA population derived from at least one uncultivated microorganism; and (ii) transforming a host with recovered DNA to produce a library of clones which is screened for the specified protein, e.g. enzyme, activity.

25 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

☐ 36. Document ID: US 6503741 B1

L3: Entry 36 of 76 File: USPT Jan 7, 2003

US-PAT-NO: 6503741
DOCUMENT-IDENTIFIER: US 6503741 B1

TITLE: Polyketide synthase genes from Streptomyces venezuelae

DATE-ISSUED: January 7, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ashley; Gary	Alameda	CA		
Betlach; Melanie C.	Burlingame	CA		
Betlach; Mary	San Francisco	CA		
McDaniel; Robert	Palo Alto	CA		
Tang; Li	Foster City	CA		

US-CL-CURRENT: 435/183; 435/189, 435/193, 435/232, 435/252.33, 435/252.35,

435/254.2, 435/320.1, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Combinatorial libraries of polyketides can be obtained by suitable manipulation of a host modular polyketide synthase gene cluster such as that which encodes the PKS for picromycin. The combinatorial library is useful as a source of pharmaceutically active compounds. In addition, novel polyketides and antibiotics are prepared using this method.

16 Claims, 37 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 30

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. De

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☐ 37. Document ID: US 6489145 B1

L3: Entry 37 of 76 File: USPT Dec 3, 2002

US-PAT-NO: 6489145
DOCUMENT-IDENTIFIER: US 6489145 B1

TITLE: Method of DNA shuffling

DATE-ISSUED: December 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/91.1

ABSTRACT:

Disclosed is a method of producing random polynucleotides by introducing two or more related polynucleotides into a suitable host cell such that a hybrid polynucleotide is generated by recombination and reductive reassortment. Also provided are vector and expression vehicles including such polynucleotides, polypeptides expressed by the hybrid polynucleotides and a method for screening for hybrid polypeptides.

24 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. De

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☐ 38. Document ID: US 6479258 B1

L3: Entry 38 of 76 File: USPT Nov 12, 2002

US-PAT-NO: 6479258
DOCUMENT-IDENTIFIER: US 6479258 B1

TITLE: Non-stochastic generation of genetic vaccines

DATE-ISSUED: November 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

This invention provides methods of obtaining vaccines by use of non-stochastic methods of directed evolution (DirectEvolution.TM.). These methods include non-stochastic polynucleotide site-satuaration mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). Through use of the claimed methods, vectors can be obtained which exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like.

86 Claims, 66 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 61

☐ 39. Document ID: US 6461838 B2

L3: Entry 39 of 76 File: USPT Oct 8, 2002

US-PAT-NO: 6461838
DOCUMENT-IDENTIFIER: US 6461838 B2

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: October 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB
Ebert-Khosla; Suzanne	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		
Fu; Hong	Stanford	CA		
Kao; Camilla	Stanford	CA		

US-CL-CURRENT: 435/91.1; 435/183, 435/252.31, 435/252.33, 435/320.1, 536/23.1,

536/23.2

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

12 Claims, 33 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 40. Document ID: US 6455254 B1

L3: Entry 40 of 76 File: USPT Sep 24, 2002

US-PAT-NO: 6455254
DOCUMENT-IDENTIFIER: US 6455254 B1
**** See image for Certificate of Correction ****

TITLE: Sequence based screening

DATE-ISSUED: September 24, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/6; 435/91.2, 536/23.1, 536/24.3, 536/24.33

ABSTRACT:

Provided is a method of obtaining a nucleic acid profile of a sample. The method includes creating a DNA library from a plurality of nucleic acid sequences of a mixed population of organisms and sequencing at least one clone in the DNA library. The sequence is compared to a database and identifying sequences in the database which have homology to a clone in the library thereby obtaining a nucleic acid profile of the mixed population of organisms.

30 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 41. Document ID: US 6444426 B1

L3: Entry 41 of 76 File: USPT Sep 3, 2002

US-PAT-NO: 6444426
DOCUMENT-IDENTIFIER: US 6444426 B1

TITLE: Production and use of normalized DNA libraries

DATE-ISSUED: September 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Sante Fe	CA		
Mathur; Eric J.	Carlsbad	CA		

US-CL-CURRENT: 435/6; 435/440, 435/91.2, 536/25.4, 536/25.42

ABSTRACT:

Disclosed is a process for forming a normalized genomic DNA library from an environmental sample by (a) isolating a genomic DNA population from the environmental sample; (b) at least one of (i) amplifying the copy number of the DNA population so isolated and (ii) recovering a fraction of the isolated genomic DNA having a desired characteristic; and (c) normalizing the representation of various DNAs within the genomic DNA population so as to form a normalized library of genomic DNA from the environmental sample. Also disclosed is a normalized genomic DNA library formed from an environmental sample by the process.

19 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

☐ 42. Document ID: US 6437151 B2

L3: Entry 42 of 76 File: USPT Aug 20, 2002

US-PAT-NO: 6437151
DOCUMENT-IDENTIFIER: US 6437151 B2

TITLE: Erythromycins and process for their preparation

DATE-ISSUED: August 20, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leadlay; Peter Francis	Cambridge			GB
Staunton; James	Cambridge			GB
Cortes; Jesus	Cambridge			GB
Pacey; Michael Stephen	Broadstairs			GB

US-CL-CURRENT: 549/271; 536/7.2, 549/13, 549/266, 549/29

ABSTRACT:

Erythromycins, particularly ones with novel C-13 substituents R1 (e.g. C.sub.3 - C.sub.6 cycloalkyl or cycloalkenyl groups) are prepared by fermenting suitable organisms in the presence of R.sub.1 CO.sub.2 H. A preferred organism is Saccharopolyspora erythraea preferably containing an integrated plasmid capable of directing synthesis of desired compounds.

10 Claims, 16 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 43. Document ID: US 6399382 B1

L3: Entry 43 of 76 File: USPT Jun 4, 2002

US-PAT-NO: 6399382
DOCUMENT-IDENTIFIER: US 6399382 B1
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: June 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB
Ebert-Khosla; Susanne	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		
Kao; Camilla	Stanford	CA		

US-CL-CURRENT: 435/440; 435/183, 435/189, 435/232, 435/252.3, 435/252.35, 435/320.1, 435/471, 435/486

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

15 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 44. Document ID: US 6391594 B1

L3: Entry 44 of 76 File: USPT May 21, 2002

US-PAT-NO: 6391594
DOCUMENT-IDENTIFIER: US 6391594 B1

TITLE: Modified modular PKS with retained scaffold

DATE-ISSUED: May 21, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Ashley; Gary	Alameda	CA		
Fu; Hong	Stanford	CA		
Kao; Camilla M.	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		

US-CL-CURRENT: 435/91.4; 435/183, 435/193, 435/252.35, 435/320.1, 435/455, 435/471, 435/486, 536/23.2

ABSTRACT:

Combinatorial libraries of polyketides can be obtained by suitable manipulation of a host modular polyketide synthase gene cluster such as that which encodes the PKS for erythromycin. The combinatorial library is useful as a source of pharmaceutically active compounds.

16 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 45. Document ID: US 6368798 B1

L3: Entry 45 of 76 File: USPT Apr 9, 2002

US-PAT-NO: 6368798
DOCUMENT-IDENTIFIER: US 6368798 B1

TITLE: Screening for novel bioactivities

DATE-ISSUED: April 9, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/6; 435/91.2

ABSTRACT:

Disclosed is a process for identifying clones having a specified enzyme activity by screening for the specified enzyme activity in a library of clones prepared by (i) selectively isolating target nucleic acid from nucleic acid derived from at least one microorganism, by use of at least one polynucleotide probe comprising at least a portion of a nucleic acid sequence encoding an enzyme having the specified enzyme activity; and (ii) transforming a host with isolated target nucleic acid to produce a library of clones which are screened for the specified enzyme activity.

50 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

☐ 46. Document ID: US 6361974 B1

L3: Entry 46 of 76 File: USPT Mar 26, 2002

US-PAT-NO: 6361974
DOCUMENT-IDENTIFIER: US 6361974 B1
**** See image for Certificate of Correction ****

TITLE: Exonuclease-mediated nucleic acid reassembly in directed evolution

DATE-ISSUED: March 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		
Djavakhishvili; Tsotne David	San Diego	CA		
Frey; Gerhard Johann	San Diego	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of exonuclease-mediated reassembly methods is the ability to reassemble nucleic acid strands that would otherwise be problematic to chimerize. Exonuclease-mediated reassembly methods can be used in combination with other mutagenesis methods provided herein. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety

of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

15 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

☐ 47. Document ID: US 6358709 B1

L3: Entry 47 of 76 File: USPT Mar 19, 2002

US-PAT-NO: 6358709
DOCUMENT-IDENTIFIER: US 6358709 B1

TITLE: End selection in directed evolution

DATE-ISSUED: March 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		
Frey; Gerhard Johann	San Diego	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

This invention provides methods of obtaining novel polynucleotides and encoded polypeptides by the use of non-stochastic methods of directed evolution (DirectEvolution.TM.). A particular advantage of end-selection-based methods is the ability to recover full-length polynucleotides from a library of progeny molecules generated by mutagenesis methods. These methods include non-stochastic polynucleotide site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This invention provides methods of obtaining novel enzymes that have optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

36 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 48. Document ID: US 6352842 B1

L3: Entry 48 of 76 File: USPT Mar 5, 2002

US-PAT-NO: 6352842
DOCUMENT-IDENTIFIER: US 6352842 B1
** See image for Certificate of Correction **

TITLE: Exonucease-mediated gene assembly in directed evolution

DATE-ISSUED: March 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		
Frey; Gerhard J.	San Diego	CA		
Djavakhishvili; Tsotne D.	San Diego	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

A directed evolution process comprising novel methods for generating improved progeny molecules having desirable properties, including, for example, a method for rapid and facilitated production from a parental polynucleotide template, of a set of mutagenized progeny polynucleotides wherein at least one codon encoding each of the 20 naturally encoded amino acids is represented at each original codon position. This method, termed site-saturation mutagenesis, or simply saturation mutagenesis, is preferably based on the use of the degenerate N,N,G/T sequence. Also, a method of producing from a parental polypeptide template, a set of mutagenized progeny polypeptides wherein each of the 20 naturally encoded amino acids is represented at each original amino acid position. Also, other mutagenization processes that can be used in combination with, or in lieu of, saturation mutagenesis, including, for example: (a) assembly and/or reassembly of polynucloetide building blocks (including sections of genes &/or of gene families) mediated by a source of exonuclease activity such as exonuclease III; and (b) introduction of two or more related polynucleotides into a suitable host cell such that a hybrid polynucleotide is generated by recombination and reductive reassortment. Also molecular property screening methods, including a preferred method, termed end selection, comprised of using an enzyme, such as a topoisomerase, a restriction endonuclease, &/or a nicking enzyme (such as N. BstNB I), to detect a specific terminal sequence in a working polynucleotide, to produce a ligatable end thereat, and to ligate and clone the working polynucleotide.

20 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

☐ 49. Document ID: US 6344328 B1

L3: Entry 49 of 76 File: USPT Feb 5, 2002

US-PAT-NO: 6344328
DOCUMENT-IDENTIFIER: US 6344328 B1
** See image for Certificate of Correction **

TITLE: Method for screening for enzyme activity

DATE-ISSUED: February 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/6; 435/91.2

ABSTRACT:

Disclosed is a process for identifying clones having a specified enzyme activity by screening for the specified enzyme activity in a library of clones prepared by (i) selectively isolating target DNA from DNA derived from at least one microorganism, by use of at least one probe DNA comprising at least a portion of a DNA sequence encoding an enzyme having the specified enzyme activity; and (ii) transforming a host with isolated target DNA to produce a library of clones which are screened for the specified enzyme activity.

24 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KMC | Draw. De

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☐ 50. Document ID: US 6280926 B1

L3: Entry 50 of 76 File: USPT Aug 28, 2001

US-PAT-NO: 6280926
DOCUMENT-IDENTIFIER: US 6280926 B1
** See image for Certificate of Correction **

TITLE: Gene expression library produced from DNA from uncultivated microorganisms and methods for making the same

DATE-ISSUED: August 28, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Rancho Santa Fe	CA		

US-CL-CURRENT: 435/4; 435/183, 435/6

ABSTRACT:

Disclosed is a process of screening clones having DNA from an uncultivated microorganism for a specified protein, e.g. enzyme, activity by screening for a specified protein, e.g. enzyme, activity in a library of clones prepared by (i) recovering DNA from a DNA population derived from at least one uncultivated microorganism; and (ii) transforming a host with recovered DNA to produce a library of clones which is screened for the specified protein, e.g. enzyme, activity.

22 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. De

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☐ 51. Document ID: US 6274560 B1

L3: Entry 51 of 76 File: USPT Aug 14, 2001

US-PAT-NO: 6274560
DOCUMENT-IDENTIFIER: US 6274560 B1

TITLE: Cell-free synthesis of polyketides

DATE-ISSUED: August 14, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Pieper; Rembert	Washington	DC		
Luo; Guanglin	Madison	CT		
Cane; David E.	Providence	RI		
Kao; Camilla	Palo Alto	CA		

US-CL-CURRENT: 514/29; 435/252.3, 435/252.35, 435/320.1, 435/471

ABSTRACT:

Cell-free systems which effect the production of polyketides employing modular polyketide synthases are described. Libraries of new and/or known polyketides may also be produced in cell-free systems employing aromatic PKS, modular PKS or both.

13 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. De

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☐ 52. Document ID: US 6271255 B1

L3: Entry 52 of 76 File: USPT Aug 7, 2001

US-PAT-NO: 6271255
DOCUMENT-IDENTIFIER: US 6271255 B1

TITLE: Erythromycins and process for their preparation

DATE-ISSUED: August 7, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leadlay; Peter Francis	Cambridge			GB
Staunton; James	Cambridge			GB
Cortes; Jesus	Cambridge			GB
Pacey; Michael Stephen	Broadstairs			GB

US-CL-CURRENT: 514/450; 514/29, 536/7.2, 549/13, 549/266, 549/271, 549/29

ABSTRACT:

Erythromycins, particularly with C-13 substituents R1 (e.g. C.sub.3 -C.sub.6 cycloalkyl or cycloalkenyl groups) are prepared by fermenting suitable organisms in the presence of R.sub.1 CO.sub.2 H. A preferred organism is Saccharopolyspora erythraea preferably containing an integrated plasmid capable of directing synthesis of desired compounds.

27 Claims, 16 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

☐ 53. Document ID: US 6238884 B1

L3: Entry 53 of 76 File: USPT May 29, 2001

US-PAT-NO: 6238884
DOCUMENT-IDENTIFIER: US 6238884 B1

TITLE: End selection in directed evolution

DATE-ISSUED: May 29, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		
Frey; Gerhard Johann	San Diego	CA		

US-CL-CURRENT: 435/69.1; 530/350, 536/23.2

ABSTRACT:

A directed evolution process comprising novel methods for generating improved

progeny molecules having desirable properties, including, for example, a method for rapid and facilitated production from a parental polynucleotide template, of a set of mutagenized progeny polynucleotides wherein at least one codon encoding each of the 20 naturally encoded amino acids is represented at each original codon position. This method, termed site-saturation mutagenesis, or simply saturation mutagenesis, is preferably based on the use of the degenerate N,N,G/T sequence. Also, a method of producing from a parental polypeptide template, a set of mutagenized progeny polypeptides wherein each of the 20 naturally encoded amino acids is represented at each original amino acid position. Also, other mutagenization processes that can be used in combination with, or in lieu of, saturation mutagenesis, including, for example: (a) assembly and/or reassembly of polynucloetide building blocks, which building blocks can be sections of genes &/or of gene families; and (b) introduction of two or more related polynucleotides into a suitable host cell such that a hybrid polynucleotide is generated by recombination and reductive reassortment. Also, vector and expression vehicles including such polynucleotides and correspondingly expressed polypeptides. Also molecular property screening methods, including a preferred method, termed end selection, comprised of using an enzyme, such as a topoisomerase, a restriction endonuclease, &/or a nicking enzyme (such as N. BstNB I), to detect a specific terminal sequence in a working polynucleotide, to produce a ligatable end thereat, and to ligate and clone the working polynucleotide.

21 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

☐ 54. Document ID: US 6215007 B1

L3: Entry 54 of 76 File: USPT Apr 10, 2001

US-PAT-NO: 6215007
DOCUMENT-IDENTIFIER: US 6215007 B1
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: April 10, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB
Ebert-Khosla; Suzanne	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		
Fu; Hong	Stanford	CA		

US-CL-CURRENT: 549/417; 549/389, 549/400, 560/128, 562/433, 562/435, 562/461

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known

polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

20 Claims, 32 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 55. Document ID: US 6214573 B1

L3: Entry 55 of 76 File: USPT Apr 10, 2001

US-PAT-NO: 6214573
DOCUMENT-IDENTIFIER: US 6214573 B1

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: April 10, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB
Ebert-Khosla; Suzanne	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		
Fu; Hong	Stanford	CA		

US-CL-CURRENT: 435/41; 435/132, 435/133, 435/147, 435/148, 435/252.3, 435/252.33, 435/252.35

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

21 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 56. Document ID: US 6174673 B1

L3: Entry 56 of 76 File: USPT Jan 16, 2001

US-PAT-NO: 6174673

DOCUMENT-IDENTIFIER: US 6174673 B1

TITLE: High throughput screening for novel enzymes

DATE-ISSUED: January 16, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		
Keller; Martin	San Diego	CA		

US-CL-CURRENT: 435/6; 435/320.1, 435/440, 435/471, 435/476, 435/69.1

ABSTRACT:

Disclosed is a process for identifying clones having a specified activity of interest, which process comprises (i) generating one or more expression libraries derived from nuclei acid directly isolated from the environment; and (ii) screening said libraries utilizing a fluorescence activated cell sorter to identify said clones. More particularly, this is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; (ii) exposing said libraries to a particular substrate or substrates of interest; and (iii) screening said exposed libraries utilizing a fluorescence activated cell sorter to identify clones which react with the substrate or substrates. Also provided is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; and (ii) screening said exposed libraries utilizing an assay requiring co-encapsulation, a binding event or the covalent modification of a target, and a fluorescence activated cell sorter to identify positive clones.

23 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

☐ 57. Document ID: US 6171820 B1

L3: Entry 57 of 76 File: USPT Jan 9, 2001

US-PAT-NO: 6171820
DOCUMENT-IDENTIFIER: US 6171820 B1
**** See image for Certificate of Correction ****

TITLE: Saturation mutagenesis in directed evolution

DATE-ISSUED: January 9, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/69.1; 435/69.7, 435/7.6, 530/350

ABSTRACT:

Disclosed is a rapid and facilitated method of producing from a parental template polynucleotide, a set of mutagenized progeny polynucleotides whereby at each original codon position there is produced at least one substitute codon encoding each of the 20 naturally encoded amino acids. Accordingly, there is also provided a method of producing from a parental template polypeptide, a set of mutagenized progeny polypeptides wherein each of the 20 naturally encoded amino acids is represented at each original amino acid position. The method provided is termed site-saturation mutagenesis, or simply saturation mutagenesis, and can be used in combination with other mutagenization processes, such as, for example, a process wherein two or more related polynucleotides are introduced into a suitable host cell such that a hybrid polynucleotide is generated by recombination and reductive reassortment. Also provided are vector and expression vehicles including such polynucleotides, polypeptides expressed by the hybrid polynucleotides and a method for screening for hybrid polypeptides.

13 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. De

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☐ 58. Document ID: US 6168919 B1

L3: Entry 58 of 76 File: USPT Jan 2, 2001

US-PAT-NO: 6168919
DOCUMENT-IDENTIFIER: US 6168919 B1

TITLE: Screening methods for enzymes and enzyme kits

DATE-ISSUED: January 2, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/6; 435/183, 435/252.3, 435/320.1, 435/325, 435/4, 435/91.1, 435/91.4, 435/91.41, 536/23.1, 536/23.2, 536/23.4

ABSTRACT:

Recombinant enzyme libraries and kits where a plurality of enzymes are each characterized by different physical and/or chemical characteristics and classified by common characteristics. The characteristics are determined by screening of recombinant enzymes expressed by a DNA library produced from various microorganisms. Also disclosed is a process for identifying clones of a recombinant library which express a protein with a desired ctivity by screening a library of expression clones randomly produced from DNA of at least one microorganism, said screeing being effected on expression products of said clones to thereby identify clones which express a protein with a desired activity. Also disclosed is a process

of screening clones having DNA from an uncultivated microorganism for a specified protein activity by screening for a specified protein activity in a library of clones prepared by (I) recovering DNA from a DNA population derived from at least one uncultivated microorganism; and (ii) transforming a host with recovered DNA to produce a library of clones which is screened for the specified protein activity.

9 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 59. Document ID: US 6080555 A

L3: Entry 59 of 76 File: USPT Jun 27, 2000

US-PAT-NO: 6080555
DOCUMENT-IDENTIFIER: US 6080555 A

TITLE: Synthesis of polyketides from diketides

DATE-ISSUED: June 27, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Pieper; Rembert	Washington	DC		
Luo; Guanglin	Providence	RI		
Cane; David E.	Providence	RI		

US-CL-CURRENT: 435/41; 435/64, 435/7.1

ABSTRACT:

Cell-free systems which effect the production of polyketides employing modular polyketide synthases are described. Libraries of new and/or known polyketides may also be produced in cell-free systems employing aromatic PKS, modular PKS or both.

14 Claims, 8 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 60. Document ID: US 6077696 A

L3: Entry 60 of 76 File: USPT Jun 20, 2000

US-PAT-NO: 6077696
DOCUMENT-IDENTIFIER: US 6077696 A

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: June 20, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB
Ebert-Khosla; Suzanne	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		
Fu; Hong	Stanford	CA		
Kao; Camilla	Stanford	CA		

US-CL-CURRENT: 435/135; 435/132, 435/147, 435/148, 435/183, 435/252.3, 435/252.33, 435/252.35, 435/320.1, 536/23.1, 536/23.2

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

6 Claims, 33 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

Terms	Documents
monensin same (gene cluster or polyketide synthase)	76

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☐ 61. Document ID: US 6057103 A

Using default format because multiple data bases are involved.

L3: Entry 61 of 76 File: USPT May 2, 2000

US-PAT-NO: 6057103
DOCUMENT-IDENTIFIER: US 6057103 A
** See image for Certificate of Correction **

TITLE: Screening for novel bioactivities

DATE-ISSUED: May 2, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/6; 435/91.1, 435/91.2, 436/501, 536/23.1, 536/24.3, 536/24.31, 536/24.32, 536/24.33, 536/25.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

☐ 62. Document ID: US 6054267 A

L3: Entry 62 of 76 File: USPT Apr 25, 2000

US-PAT-NO: 6054267
DOCUMENT-IDENTIFIER: US 6054267 A
** See image for Certificate of Correction **

TITLE: Method for screening for enzyme activity

DATE-ISSUED: April 25, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinias	CA		

US-CL-CURRENT: 435/6; 435/69.1

ABSTRACT:

Disclosed is a process for identifying clones having a specified enzyme activity by

screening for the specified enzyme activity in a library of clones prepared by (i) selectively isolating target DNA from DNA derived from at least one microorganism, by use of at least one probe DNA comprising at least a portion of a DNA sequence encoding an enzyme having the specified enzyme activity; and (ii) transforming a host with isolated target DNA to produce a library of clones which are screened for the specified enzyme activity.

24 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

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☐ 63. Document ID: US 6030779 A

L3: Entry 63 of 76 File: USPT Feb 29, 2000

US-PAT-NO: 6030779
DOCUMENT-IDENTIFIER: US 6030779 A

TITLE: Screening for novel bioactivities

DATE-ISSUED: February 29, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/6; 435/91.2

ABSTRACT:

Disclosed is a process for identifying clones having a specified enzyme activity by screening for the specified enzyme activity in a library of clones prepared by (i) selectively isolating target nucleic acid from nucleic acid derived from at least one microorganism, by use of at least one polynucleotide probe comprising at least a portion of a nucleic acid sequence encoding an enzyme having the specified enzyme activity; and (ii) transforming a host with isolated target nucleic acid to produce a library of clones which are screened for the specified enzyme activity.

38 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

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☐ 64. Document ID: US 6022731 A

L3: Entry 64 of 76 File: USPT Feb 8, 2000

US-PAT-NO: 6022731

DOCUMENT-IDENTIFIER: US 6022731 A

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: February 8, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB
Ebert-Khosla; Suzanne	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		

US-CL-CURRENT: 435/252.35; 435/252.3, 435/252.33, 435/320.1, 435/471, 435/476, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

45 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

☐ 65. Document ID: US 6001574 A

L3: Entry 65 of 76 File: USPT Dec 14, 1999

US-PAT-NO: 6001574
DOCUMENT-IDENTIFIER: US 6001574 A

TITLE: Production and use of normalized DNA libraries

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		
Mathur; Eric J.	Carlsbad	CA		

US-CL-CURRENT: 435/6; 435/440, 435/91.2, 536/25.4, 536/25.42

ABSTRACT:

Disclosed is a process for forming a normalized genomic DNA library from an environmental sample by (a) isolating a genomic DNA population from the

environmental sample; (b) at least one of (i) amplifying the copy number of the DNA population so isolated and (ii) recovering a fraction of the isolated genomic DNA having a desired characteristic; and (c) normalizing the representation of various DNAs within the genomic DNA population so as to form a normalized library of genomic DNA from the environmental sample. Also disclosed is a normalized genomic DNA library formed from an environmental sample by the process.

14 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

☐ 66. Document ID: US 5986077 A

L3: Entry 66 of 76 File: USPT Nov 16, 1999

US-PAT-NO: 5986077
DOCUMENT-IDENTIFIER: US 5986077 A

TITLE: Process for producing anthracyclines and intermediates thereof

DATE-ISSUED: November 16, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ylihonko; Kristiina	Turku			FI
Hakala; Juha	Turku			FI
Mantsala; Pekka	Turku			FI

US-CL-CURRENT: 536/23.1; 435/128, 435/320.1, 435/41

ABSTRACT:

A process for producing anthracyclines and intermediates thereof expressing in a foreign Streptomyces host a DNA fragment relating to the biosynthetic pathway of anthracyclines and, if desired, intermediates obtained may be converted to anthracyclines or aglycones thereof using e.g. non-producing Streptomyces mutant strains.

14 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

☐ 67. Document ID: US 5962290 A

L3: Entry 67 of 76 File: USPT Oct 5, 1999

US-PAT-NO: 5962290
DOCUMENT-IDENTIFIER: US 5962290 A

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: October 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB
Ebert-Khosla; Suzanne	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		
Fu; Hong	Stanford	CA		
Kao; Camilla	Stanford	CA		

US-CL-CURRENT: 435/183; 435/252.3, 435/252.33, 435/252.35, 435/320.1, 435/471, 435/476, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

21 Claims, 33 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

☐ 68. Document ID: US 5958672 A

L3: Entry 68 of 76 File: USPT Sep 28, 1999

US-PAT-NO: 5958672
DOCUMENT-IDENTIFIER: US 5958672 A

TITLE: Protein activity screening of clones having DNA from uncultivated microorganisms

DATE-ISSUED: September 28, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/4; 435/183, 435/69.1, 536/23.1, 536/23.2

ABSTRACT:

Disclosed is a process of screening clones having DNA from an uncultivated microorganism for a specified protein, e.g. enzyme, activity by screening for a specified protein, e.g. enzyme, activity in a library of clones prepared by (i) recovering DNA from a DNA population derived from at least one uncultivated microorganism; and (ii) transforming a host with recovered DNA to produce a library of clones which is screened for the specified protein, e.g. enzyme, activity.

15 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 69. Document ID: US 5939250 A

L3: Entry 69 of 76 File: USPT Aug 17, 1999

US-PAT-NO: 5939250
DOCUMENT-IDENTIFIER: US 5939250 A

TITLE: Production of enzymes having desired activities by mutagenesis

DATE-ISSUED: August 17, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		

US-CL-CURRENT: 435/4; 435/183, 435/69.1, 536/23.1, 536/23.2

ABSTRACT:

Disclosed is a process for obtaining an enzyme having a specified enzyme activity derived from a heterogeneous DNA population by screening, for the specified enzyme activity, a library of clones containing DNA from the heterogeneous DNA population which have been exposed to directed mutagenesis towards production of the specified enzyme activity. Also disclosed is a process for obtaining an enzyme having a specified enzyme activity by screening, for the specified enzyme activity, a library of clones containing DNA from a pool of DNA populations which have been exposed to directed mutagenesis in an attempt to produce in the library of clones DNA encoding an enzyme having one or more desired characteristics which can be the same or different from the specified enzyme activity.

12 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 70. Document ID: US 5843718 A

L3: Entry 70 of 76 File: USPT Dec 1, 1998

US-PAT-NO: 5843718
DOCUMENT-IDENTIFIER: US 5843718 A
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: December 1, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB2
Ebert-Khosla; Susanne	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		
Fu; Hong	Stanford	CA		

US-CL-CURRENT: 435/69.1; 435/183, 435/252.3, 435/325

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

21 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

☐ 71. Document ID: US 5830750 A

L3: Entry 71 of 76 File: USPT Nov 3, 1998

US-PAT-NO: 5830750
DOCUMENT-IDENTIFIER: US 5830750 A
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB2
Ebert-Khosla; Suzanne	Stanford	CA		

US-CL-CURRENT: 435/252.35; 435/252.3, 435/254.11, 435/325

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

8 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 72. Document ID: US 5763239 A

L3: Entry 72 of 76 File: USPT Jun 9, 1998

US-PAT-NO: 5763239
DOCUMENT-IDENTIFIER: US 5763239 A

TITLE: Production and use of normalized DNA libraries

DATE-ISSUED: June 9, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Short; Jay M.	Encinitas	CA		
Mathur; Eric J.	Carlsbad	CA		

US-CL-CURRENT: 435/6; 435/489, 435/91.2, 536/25.4

ABSTRACT:

Disclosed is a process for forming a normalized genomic DNA library from an environmental sample by (a) isolating a genomic DNA population from the environmental sample; (b) analyzing the complexity of the genomic DNA population so isolated; (c) at least one of (i) amplifying the copy number of the DNA population so isolated and (ii) recovering a fraction of the isolated genomic DNA having a desired characteristic; and (d) normalizing the representation of various DNAs within the genomic DNA population so as to form a normalized library of genomic DNA from the environmental sample. Also disclosed is a normalized genomic DNA library formed from an environmental sample by the process.

14 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 73. Document ID: US 5712146 A

L3: Entry 73 of 76 File: USPT Jan 27, 1998

US-PAT-NO: 5712146
DOCUMENT-IDENTIFIER: US 5712146 A
**** See image for Certificate of Correction ****

TITLE: Recombinant combinatorial genetic library for the production of novel polyketides

DATE-ISSUED: January 27, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Khosla; Chaitan	Stanford	CA		
Hopwood; David A.	Norwich			GB2
Ebert-Khosla; Suzanne	Stanford	CA		
McDaniel; Robert	Palo Alto	CA		
Fu; Hong	Stanford	CA		
Kao; Camilla	Stanford	CA		

US-CL-CURRENT: 435/252.35; 435/148, 435/156, 435/252.3, 435/252.33, 435/320.1, 536/23.1, 536/23.2, 536/23.7

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

5 Claims, 33 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 26

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 74. Document ID: US 5672491 A

L3: Entry 74 of 76 File: USPT Sep 30, 1997

US-PAT-NO: 5672491
DOCUMENT-IDENTIFIER: US 5672491 A
**** See image for Certificate of Correction ****

TITLE: Recombinant production of novel polyketides

DATE-ISSUED: September 30, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY

Khosla; Chaitan	Stanford	CA	
Hopwood; David A.	Norwich		GB2
Ebert-Khosla; Suzanne	Stanford	CA	
McDaniel; Robert	Palo Alto	CA	
Fu; Hong	Stanford	CA	
Kao; Camilla	Stanford	CA	

US-CL-CURRENT: 435/148; 435/183, 435/252.35, 435/320.1, 435/76, 435/91.4

ABSTRACT:

Novel polyketides and novel methods of efficiently producing both new and known polyketides, using recombinant technology, are disclosed. In particular, a novel host-vector system is described which is used to produce polyketide synthases which in turn catalyze the production of a variety of polyketides.

24 Claims, 15 Drawing figures
Exemplary Claim Number: 15
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. De

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☐ 75. Document ID: US 20040219645 A1, WO 200168867 A1, AU 200049408 A, EP 1183369 A1

L3: Entry 75 of 76 File: DWPI Nov 4, 2004

DERWENT-ACC-NO: 2001-611393
DERWENT-WEEK: 200473
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TITLE: New DNA sequence encoding polyketide synthase, useful for the production of polyketides such as antibiotic monensin

INVENTOR: LEADLAY, P F; OLIYNYK, M ; STAUNTON, J ; LEADLEY, P F ; OLIYNYK, M Y

PRIORITY-DATA: 1999GB-0012563 (May 28, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 20040219645 A1	November 4, 2004		000	C12P019/62
WO 200168867 A1	September 20, 2001	E	109	C12N015/52
AU 200049408 A	September 24, 2001		000	C12N015/52
EP 1183369 A1	March 6, 2002	E	000	C12N015/52

INT-CL (IPC): C07 H 17/08; C07 H 19/01; C12 N 15/52; C12 N 15/76; C12 P 17/18; C12 P 19/44; C12 P 19/62; C12 Q 1/68

ABSTRACTED-PUB-NO: WO 200168867A
BASIC-ABSTRACT:

NOVELTY - A DNA sequence (Ia) which is a fully defined sequence of 103551 base pairs as given in the specification or a variant of the sequence that encodes a polypeptide that is at least 80%, preferably at least 90% identical with the corresponding peptide fully defined in the specification, provided that it is not a sequence encoding all or part of the polypeptide consisting of amino acids 1-920 encoded by mon AI as given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a DNA sequence (Ib) encoding at least part of a polypeptide which is necessary for the biosynthesis of monensin and is encoded by DNA fully defined in the specification or an allele, mutation or other variant, provided that the polypeptide is not all or part of amino acids 1-920 encoded by mon AI as given in the specification;

(2) a recombinant cloning or expression vector comprising (Ia) or (Ib);

(3) a transformant host cell which has been transformed to contain (Ia) or (Ib) and is capable of expressing a corresponding polypeptide;

(4) a hybridization probe (II) which is (Ia) or (Ib);

(5) use (M1) of (II) to detect polyketide synthase (PKS) cluster, optionally followed by isolation of the detected cluster;

(6) use of (II) to detect genes encoding polypeptides having analogous function;

(7) use (M2) of (II) to detect an analogous gene in a gene cluster for biosynthesis of another polyketide, optionally followed by manipulating the gene detected to alter the level of expression of the other polyketide;

(8) a hybridization probe (III) comprising a polynucleotide that binds specifically to a region of the monensin gene cluster selected from mon BI, mon BII, mon CI, mon CII, mon H, Mon RI, mon RII, mon T, mon AIX and mon AX;

(9) use of (III) to detect the presence of a gene cluster which governs the synthesis of a polyether and optionally isolating a gene cluster detected;

(10) use of the mon RI gene or variant and a monensin promoter to control expression of a heterologous gene in Streptomyces cinnamonensis;

(11) a polypeptide (III) encoded by a portion of the monensin gene cluster, preferably comprising:

(a) mon BI and mon BII or their mutants, alleles or variants, having carbon-carbon double bond isomerase activity; or

(b) mon AIX and mon AX or their mutants, alleles or variants, having chain terminating activity;

(12) use of a portion of the monensin gene cluster encoding (III) to effect chain release of a non-monensin peptide and provide a desired stereochemical outcome in the synthesis of a non-monensin polyketide;

(13) an epoxidase enzyme encoded by mon CI or its derivative or variant having epoxidase activity;

(14) a cyclase enzyme encoded by mon CII or its derivative or variant having cyclase activity;

(15) use of a portion of the monensin gene cluster encoding an epoxidase or cyclase enzyme to provide the activity in the biosynthesis of a non-monensin polypeptide;

(16) producing (M3) a polyketide containing a desired starter unit comprising providing a PKS gene having a loading molecule and a number of extension nodules, where the loading molecule includes a KSq domain derived from a KS domain of a monensin extension module;

(17) a DNA sequence (IV) encoding at least one PKS loading molecule and a number of PKS extension modules and can be expressed to produce a polyketide;

(18) a PKS (V) encoded by (IV);

(19) a polyketide compound produced by (V);

(20) a vector containing (IV);

(21) a transformant cell transformed to contain (IV);

(22) producing (M4) S. cinnamonensis capable of enhanced levels of production of monensin comprising engineering it to overexpress the mon RI gene;

S. cinnamonensis (VI) containing multiple copies of the mon RI gene and/or its variants;

(23) producing monensin comprising culturing (VI) or an organism produced by M4;

(24) expressing (M5) a gene heterologous to S. cinnamonensis comprising transforming S. cinnamonensis with DNA encoding a heterologous gene and expressing the gene under control of the activator gene mon RI or actII/orf4; and

(25) 13-propyl erythromycin A.

ACTIVITY - Antibiotic; anthelmintic; antifungal; antibacterial. No supporting data is given.

MECHANISM OF ACTION - None given.

USE - The processes and materials (enzyme systems, nucleic acids and vectors) are useful for preparing polyketides by recombinant synthesis. The polyketides are useful as antibiotics, anthelmintics, antifungals, antibacterials or other pharmaceuticals. In particular the gene is useful for the production of monensin, an antibiotic polyether polyketide.

☐ 76. Document ID: AU 2005202312 A1, WO 9923236 A1, AU 9912765 A, EP 1027450 A1, JP 2002505845 W, AU 200245900 A, US 6489145 B1, JP 2003245073 A, CA 2308292 C

L3: Entry 76 of 76 File: DWPI Jun 23, 2005

DERWENT-ACC-NO: 1999-313351
DERWENT-WEEK: 200545
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TITLE: Production of hybrid polynucleotides by introducing first and second polynucleotides into host cells for sequence reorganization

INVENTOR: SHORT, J M

PRIORITY-DATA: 1997US-0962504 (October 31, 1997), 2002AU-0045900 (June 11, 2002), 1996US-0677112 (July 9, 1996), 2005AU-0202312 (May 27, 2005)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 2005202312 A1	June 23, 2005		000	C12N015/85
WO 9923236 A1	May 14, 1999	E	089	C12N015/85
AU 9912765 A	May 24, 1999		000	
EP 1027450 A1	August 16, 2000	E	000	
JP 2002505845 W	February 26, 2002		099	C12N015/09
AU 200245900 A	August 1, 2002		000	C12N015/85
US 6489145 B1	December 3, 2002		000	C12P019/34
JP 2003245073 A	September 2, 2003		040	C12N015/09
CA 2308292 C	January 25, 2005	E	000	C12N015/85

INT-CL (IPC): C07 K 19/00; C12 N 1/15; C12 N 1/21; C12 N 5/10; C12 N 15/09; C12 N 15/85; C12 N 15/87; C12 P 19/34; C12 Q 1/68

ABSTRACTED-PUB-NO: WO 9923236A
BASIC-ABSTRACT:

NOVELTY - A new method for the production of hybrid polynucleotides comprises introducing first and second polynucleotides which share at least one region of partial sequence homology into host cells for sequence reorganization.

DETAILED DESCRIPTION - A novel method for producing a hybrid polynucleotide (PN) comprises:

(a) introducing at least a first PN and a second PN which share at least one region of partial sequence homology into a suitable host cell, where the regions of partial sequence homology promote processes which result in sequence reorganization;

(b) producing the hybrid PN.

INDEPENDENT CLAIMS are also included for the following:

(1) a method for producing a biologically active hybrid polypeptide and screening the polypeptide for enhanced activity, comprising:

(a) introducing at least a first PN in operable linkage and a second PN in operable linkage, the at least first PN and second PN sharing at least one region of partial sequence homology, into a suitable host cell;

(b) growing the host cell of (a) to promote sequence reorganization preferably reductive reassortment, resulting in a hybrid PN in operable linkage;

(c) expressing a hybrid polypeptide encoded by a hybrid PN of (b);

(d) screening a hybrid polypeptide of (c) to promote identification of enhanced biological activity;

(e) isolating a PN encoding a hybrid polypeptide of (d);

(2) a method for producing a hybrid PN comprising:

(a) introducing at least a first PN and a second PN which share at least one region of partial sequence homology into a suitable host cell; where the regions of partial sequence homology promote reductive reassortment; and

(b) producing the hybrid PN; and

(3) a method of screening for biologically active polypeptides encoded by PNs comprising:

(a) screening for the activity of a hybrid polypeptide;

(b) screening for the activity of a first polypeptide;

(c) screening for the activity of a second polypeptide;

(d) comparing the activities identified in (a), (b) and (c), such that the hybrid polypeptide has enhanced activity; and

(e) isolating the PN encoding the hybrid polypeptide having enhanced activity.

USE - The methods can be used for generating hybrid PNs encoding biologically active hybrid polypeptides with enhanced activities, e.g. the original PNs may encode a particular enzyme from different microorganisms; an enzyme encoded by a first PN from one organism may for example, function effectively under a particular environmental condition, e.g. high salinity; an enzyme encoded by a second PN from a different organism may function effectively under a different environmental condition, such as extremely high temperatures; a hybrid PN containing sequences from the first and second original PNs may encode an enzyme which exhibits characteristics of both enzymes encoded by the original PNs.

Thus, the enzyme encoded by the hybrid PN may function effectively under environmental conditions shared by each of the enzymes encoded by the first and second PNs, e.g. high salinity and extreme temperatures. The enzymes may be e.g. oxidoreductases, transferases, hydrolases, lyases, isomerases and ligases.

The methods can also be used to generate novel PNs encoding biochemical pathways involving gene clusters such as those producing polyketides including antibiotics (such as tetracyclines and erythromycin), anti-cancer agents (daunomycin), immunosuppressants (FK506 and rapamycin), and veterinary products (monensin).

The methods can also be used for producing hybrid PNs for producing antibodies with desired properties.

ADVANTAGE - Using the methods, no prior information regarding an expected ligand structure is required to isolate peptide ligands or antibodies of interest. The peptide identified can have biological activity, which is meant to include at least specific binding affinity for a selected receptor molecule and, in some instances, will further include the ability to block the binding of other compounds, to stimulate or inhibit metabolic pathways, to act as a signal or messenger, or to stimulate or inhibit cellular activity.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

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Terms	Documents
monensin same (gene cluster or polyketide synthase)	76

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